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Uterine Sarcoma in the South of Israel: Study of 36 Cases

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Background: Uterine sarcomas are rare, charaterized by rapid clinical progression and poor prognosis, and their management has been a challenge. The purpose of this study was to investigate the clinical and histologic findings, treatment, and outcome of patients with uterine sarcoma in the south of Israel.

Methods: Data from the files of 36 patients with uterine sarcoma who were managed at the Soroka Medical Center between January 1961 and December 1994 were evaluated.

Results: The 5-year survival rate was 32% overall; 63% for 9 patients with endometrial stromal sarcoma (ESS), 30% for 14 patients with mixed mesodermal sarcoma (MMS) and 18% for 13 patients with leiomyosarcoma (LMS); 41% for 22 patients with Stage I and 19% for 14 patients with Stages II, III, and IV. Only the difference in the 5-year survival rate between ESS and LMS was statistically significant ($P < 0.05$). Eleven patients (30.6%) were treated with surgery alone, 4 (11.1%) with surgery followed by pelvic radiotherapy, 11 (30.6%) with surgery followed by chemotherapy, 8 (22.2%) with surgery followed by pelvic radiotherapy and chemotherapy, one (2.8%) with chemotherapy alone, and one (2.8%) had no treatment.

Conclusions: Uterine sarcomas are aggressive tumors with a poor prognosis. The treatment is surgery generally followed by adjuvant pelvic radiotherapy and/or systemic chemotherapy. J. Surg. Oncol. 64: 55–62

KEY WORDS: leiomyosarcoma; endometrial stromal sarcoma; mixed mesodermal sarcoma; carcinosarcoma; rhabdomyosarcoma; uterine corpus

INTRODUCTION

Uterine sarcomas are characterized by rapid clinical progression and poor prognosis [1–5]. They are rare, accounting for only 3–7% of malignant tumors of the uterine corpus and for only ~1% of all female genital tract malignancies, with an estimated incidence of ~1/100,000 women [1,2,5,6]. Ober and Tovel [7], in 1959, introduced an histologic classification of uterine sarcomas. However, the application of this classification has presented a problem for clinicians due to excessive detail. Consequently, a simplified histologic classification based on the three main histologic types of uterine sarcoma—leiomyosarcoma (LMS), endometrial stromal sarcoma (ESS), and mixed mesodermal sarcoma (MMS)—has

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TABLE I. Simplified Histological Classification of Uterine Sarcomas

Histologic form	Histologic type	
	Homologous	Heterologous
Pure	LMS[a]	LMS[a] with heterologous element(s): rhabdomyosarcoma, chondrosarcoma, osteosarcoma, liposarcoma.
	ESS[b]	ESS[b] with heterologous element(s): rhabdomyosarcoma, chondrosarcoma, osteosarcoma, liposarcoma.
Mixed (MMS)[c]	CS[d]	MMMMT[e]

[a]Leiomyosarcoma.
[b]Endometrial stromal sarcoma.
[c]Mixed mesodermal sarcoma.
[d]Carcinosarcoma.
[e]Malignant mullerian mixed mesodermal tumor.

been established and widely accepted [8]. MMS is usually further divided, according to the absence or presence of heterologous sarcomatous elements, into carcinosarcoma (CS) and malignant mullerian mixed mesodermal tumor (MMMMT) (Table I).

The adoption of the International Federation of Gynecology and Obstetrics (FIGO) staging of endometrial adenocarcinoma for use in uterine sarcomas has presented a problem as well [2]. Although uterine sarcomas that originate in the endometrium (ESS and MMS) can be staged surgically according to the FIGO staging system for endometrial adenocarcinoma, this is impossible with a sarcoma arising from the myometrium (LMS), since Stages I and II cannot be divided into substages. Lewis et al. [9] have consequently modified the FIGO surgical staging for endometrial adenocarcinomas and accommodated it for uterine sarcomas by omitting the substages as follows: Stage I: tumor confined to the uterine body; Stage II: tumor confined to the uterine body and cervix; Stage III: tumor spread outside the uterus, but confined to the true pelvis; Stage IV: tumor spread outside the true pelvis.

Since uterine sarcomas are uncommon and consequently very few individuals or even referral centers can build up an adequate experience of handling this disease, its optimal management has been a challenge and a subject of debate and has not yet been established [10]. Management of uterine sarcomas has traditionally followed that of endometrial adenocarcinoma with total abdominal hysterectomy and bilateral salpingo-oophorectomy being the mainstay of treatment. Adjuvant pelvic radiotherapy has generally been applied in early-stage disease, and systemic chemotherapy has generally been administered in advanced-stage disease. However, there is no definitive evidence that postoperative adjuvant pelvic radiotherapy is benificial even in preventing pelvic recurrence, and the efficacy of postoperative adjuvant systemic chemotherapy in uterine sarcomas has not yet been demonstrated [10,11].

The Soroka Medical Center (SMC) in Beer-Sheva is the only tertiary care medical facility in the south of Israel that provides hospital care for a population of ~300,000. Jews from various ethnic origins make up ~80% of the population and Arab-Beduins comprise the remaining 20%. Previously, only two reports on uterine sarcoma in Israeli patients have been published [12,13]. The aim of the present study was to report the clinical and histologic findings, treatment, and outcome of 36 patients with uterine sarcoma managed at the SMC from its inauguration in January 1961 until December 1994. During this period, 321 malignancies of the uterine corpus were diagnosed; thus 36 uterine sarcomas accounted for 11.2% of all uterine corpus malignancies.

MATERIALS AND METHODS

The clinical and pathological records of 36 patients with uterine sarcoma who were managed at the SMC between January 1961 and December 1994 were reviewed. Uterine sarcomas were separated into three main histologic types: leiomyosarcoma (LMS), endometrial stromal sarcoma (ESS), and mixed mesodermal sarcoma (MMS). The histopathologic criteria used for the diagnosis of LMS were similar to those of Hendrickson and Kempson [14] and Zaloudek and Norris [15] and included patients with >10 mitoses per 10 high-power fields (with 40 fields counted) or with a mitotic rate of 5–9 per 10 high-power fields (with 40 fields counted) and nuclear atypia or metastases. ESSs were divided, according to the histopathologic criteria of Norris and Taylor [16], into two subgroups: low-grade ESS (<10 mitotic figures/10 high-power fields) and high-grade ESS ($\geqslant$10 mitotic figures/10 high-power fields). When microscopic examination revealed an admixture of malignant sarcomatous (mesenchymal) and carcinomatous (epithelial) components, the tumor was designated as MMS [6]. MMSs were further divided, according to the absence or presence of sarcomatous heterologous elements, into two histologic subtypes: carcinosarcoma (CS) and malignant mullerian mixed mesodermal tumor (MMMMT), respectively. Homologous element was defined as a sarcomatous tissue composed of malignant cells that are morphologically recognizable as being derived from mesenchymal tissue normally present in the uterus. Heterologous element was defined as a sarcomatous tissue composed of malignant cells that are differentiated into mesenchymal structures not normally present in the uterus, such as striated muscle (rhabdomyosarcoma), cartilage (chondrosarcoma), bone (osteosarcoma), and fat (liposarcoma) [6,10].

All patients were retrospectively staged according to the recently modified FIGO staging system adopted by Lewis et al [9] for uterine sarcomas after thorough record

review. For patients who had surgery, it consisted of at least total abdominal hysterectomy. For patient who received radiotherapy, it consisted of external megavoltage photonic irradiation employing a 10 MeV linear accelerator delivering 4,500–5,040 cGy to the whole pelvis in daily fractions of 180 cGy via an AP-PA opposed fields or four-field box technique. In some patients, this was followed by two intravaginal applications of brachytherapy using Cesium-137 (each application: vaginal surface dose of 2,000 cGy) via an afterloading applicator (Delclos). For patients who received systemic chemotherapy, it included various regimens: cyclophosphamide, Adriamycin and cisplatin (CAP); vincristine, Adriamycin and cyclophosphamide; cyclosphosphamide and cisplatin (CP); Adriamycin and DTIC (dimethyltriazeno-imidazole carboxamide); Adriamycin and cyclophosphamide; Adriamycin and ifosfamide; cisplatin and ifosfamide; etoposide (VP-16) and ifosfamide, Adriamycin alone; and cisplatin alone.

The following data were retrieved from the files of the patients: ethnic origin, age at initial diagnosis, pre- or postmenopausal status, gravididty, parity, history of previous malignancy, presenting symptoms, time interval from the beginning of symptoms until diagnosis of uterine sarcoma, method of diagnosis, histopathological findings, stage of disease, treatment modality (primary and adjuvant), and results of follow-up. Evaluation of statistical significance of the difference between means was performed by Student's t-test [17] and survival was calculated using the Kaplan-Meier method [18].

RESULTS

Of the 36 patients, 34 (94.4%) were Jewish and two (5.6%) were Arab-Beduin. Of the 34 Jewish patients, 21 (61.8%) were of European-American origin (Ashkenazi) and 13 (38.2%) were of Asian-African origin (Sephardic). The mean age at the time of diagnosis of all 36 patients was 60 years (range, 38–83 years). Ten patients (27.8%) were premenopausal and 26 (72.2%) were postmenopausal. One patient (2.8%) was nulliparous and 35 (97.2%) had at least one child at the time of diagnosis. The mean parity of the parous patients was 4 (range, 1–16 children). Four patients (all with MMS) had another primary malignancy prior to the uterine sarcoma (two had lymphoma and two had breast cancer), which had been successfully treated by radiotherapy and/or chemotherapy. The time interval between the previous malignancy and uterine sarcoma ranged from 9 months to 8 years.

The presenting symptoms are summarized in Table II. The most common symptom was abnormal uterine bleeding and the commonest physical sign was uterine enlargement. None of the 17 patients who presented with an enlarged uterus were recorded to have a ''fast growing uterus.'' The time interval from the beginning of symptoms until seeking medical attention was recorded in 28 patients and ranged from 1 to 24 months (mean, 3.7 months). Dilatation and curettage established the diagnosis in 19 (76%) of the 25 patients in whom it had been performed for abnormal uterine bleeding prior to explorative laparotomy. In 11 patients, dilatation and curettage had not been performed prior to explorative laparotomy.

TABLE II. Presenting Symptoms of Uterine Sarcoma

Symptom[a]	No. of patients	(%)
Postmenopausal bleeding	21	(58.3%)
Pelvic mass	17	(47.2%)
Intermenstrual bleeding and/or excessive menstrual bleeding	8	(22.2%)
Hematuria	1	(2.8%)
Retention of urine	1	(2.8%)
Constipation	1	(2.8%)

[a]Some patients presented with a combination of symptoms; therefore percentage adds up to >100%.

The distribution of patients according to modified FIGO staging and histologic type is given in Table III. Twenty-two patients (61.1%) had Stage I disease at presentation, one (2.8%) had Stage II, five (13.9%) had Stage III, and eight (22.2%) had Stage IV. The distribution of patients in relation to histologic type and presence of homologous or heterologous sarcomatous element(s) is displayed in Table IV. Thirteen patients (36.1%) had LMS (mean age at diagnosis, 52 years; range, 39–70 years), 14 patients (38.9%) had MMS (7 had CS, and 7 had MMMMT; mean age, 67 years; range, 57–78 years) and nine patients (25%) had ESS (4 had low-grade ESS and 5 had high-grade ESS; mean age, 60 years; range, 38–83 years). No significant differences in mean age at the time of diagnosis were noticed between the various histologic types (Student's *t*-test, $P > 0.05$). Of the 14 patients with MMS, the carcinomatous element was endometrioid adenocarcinoma in six patients (42.9%), adenosquamous carcinoma in four patients (28.6%), serous adenocarcinoma in two patients (14.3%), clear cell carcinoma in one patient (7.1%), and an admixture of clear cell and endometrioid carcinoma in one patient (7.1%). In nine patients the uterine sarcoma contained heterologous sarcomatous element(s): rhabdomyosarcoma alone in four patients (44.5%), chondrosarcoma alone in two patients (22.2%), osteosarcoma alone in two patients (22.2%), and an admixture of chondrosarcoma and osteosarcoma in one patient (11.1%).

Mitotic count (mitotic figures per 10 high-power fields) was recorded in 12 of 13 patients with LMS and ranged from 4 to 40 (mean, 15.2) and in all nine patients with ESS and ranged from 5 to 30 (mean, 14.9). Mitotic count was not recorded in patients with MMS. Overall, mitotic count was recorded in 21 of the 36 patients (58.3%) and ranged from 4 to 40 (mean, 15).

TABLE III. Distribution of Patients With Uterine Sarcoma According to FIGO* Staging and Histologic Type (n = 36)

Stage	Histologic type			Total	Literature[a]
	LMS	MMS	ESS		
I	10	6	6	22 (61.1%)	527 (60.2%)
II	-	1	-	1 (2.8%)	87 (9.9%)
III	1	3	1	5 (13.9%)	147 (16.8%)
IV	2	4	2	8 (22.2%)	115 (13.1%)
Total	13 (36.1%)	14 (38.9%)	9 (25%)	36 (100.0%)	876 (100.0%)
Literature[b]	617 (42.8%)	555 (38.5%)	209 (14.5%)	1440 (100.0%)	

*International Federation of Gynecology and Obstetrics. LMS, leiomyosarcoma; MMS, mixed mesodermal sarcoma; ESS, endometrial stromal sarcoma.

[a]Patients collated from six series in literature [2,5,8,12,29,30].

[b]Patients collated by Lurain and Piver [1] from 14 series in literature (4.1% of the patients had other sarcomas; therefore percentage does not add up to 100%).

TABLE IV. Distribution of Patients With Uterine Sarcoma According to Histologic Type and Presence of Homologous or Heterologous Sarcomatous Element(s) (n = 36)

Histologic type[a]	Sarcomatous element(s)		Total
	Homologous	Heterologous	
LMS	12	1	13
MMS	7 (CS)[b]	7 (MMMMT)[c]	14[d]
Low-grade ESS	4	-	4
High-grade ESS	4	1	5
Total	27	9[e]	36

[a]LMS, leiomyosarcoma; MMS, mixed mesodermal sarcoma; ESS, endometrial stromal sarcoma.

[b]Carcinosarcoma.

[c]Malignant mullerian mixed mesodermal tumor.

[d]Type of carcinomatous element: endometrioid, 6, adenosquamous, 4, serous, 2, clear cell, 1, admixture of clear cell and endometrioid, 1.

[e]Type of heterologous element: rhabdomyosarcona, 4, chondrosarcoma, 2, osteosarcoma, 2, admixture of chondrosarcoma and osteosarcoma, 1.

The distribution of treatment modalities in relation to FIGO staging and according to histologic type/subtype is displayed in Table V and Table VI, respectively. Of the 34 patients who had surgery, 27 (7 LMS, 8 ESS and 12 MMS) had total abdominal hysterectomy and bilateral salpingo-oophorectomy, one (LMS) had subtotal abdominal hysterectomy and bilateral salpingo-oophorectomy, and six (5 LMS and 1 ESS) had total abdominal hysterectomy with bilateral ovarian conservation. Of the 12 patients who had pelvic radiotherapy, in 11 patients (3 LMS, 2 ESS, and 6 MMS) it was given postoperatively as an adjuvant therapy and in one (CS) it was given preoperatively. Of the 20 patients who received systemic chemotherapy, in 19 (10 LMS, 4 ESS and 5 MMS) it was given postoperatively as an adjuvant therapy and in one (MMS) chemotherapy was the sole treatment. Of the 36 patients, one patient (with Stage IV MMMMT) had died of disease before initiation of any treatment.

Site of recurrence was documented in 18 patients. The distribution of patients according to site of recurrence is displayed in Table VII. The most common sites of locoregional recurrence were the central pelvis and vagina, whereas the most common sites for distant recurrence were the lung, abdomen, and liver. The mean recurrence-free interval was 13.3 months (16.3 months for 7 LMS patients, 8.0 months for 4 ESS patients, and 13.4 months for 7 MMS patients). No significant differences in mean recurrence-free interval were noted between the various histologic types (Student's *t*-test, $P > 0.05$).

Follow-up ranged from 1 to 299 months, with 29 (80.6%) of the 36 patients followed for at least 5 years or until time of death. None of the patients was lost to follow-up; seven patients (19.5%) were alive free of disease, four (11.1%) were alive with disease, 22 (61.1%) had died of disease, and three (8.3%) had died of intercurrent disease. The actuarial 5-year survival rate was 32% overall; 18% for the patients with LMS, 63% for the patients with ESS and 30% for the patients with MMS (Fig. 1). Only the difference in the actuarial 5-year survival rate between the patients with LMS and the patients with ESS (18% vs. 63%, respectively) was statistically significant ($P < 0.05$). The actuarial 5-year survival rate for Stage I alone was 41%, whereas that for Stages II, III, and IV combined was 19% (the difference was not statistically significant). The actuarial 5-year survival rate for the 21 patients in whom the mitotic count was recorded was 25% overall; 32% for the patients with mitotic count <15 mf/10 HPF and 20% for the patients with mitotic count equal to or more than 15 mf/10 HPF (the difference was not statistically significant). The difference in the actuarial 5-year survival rate between patients >60 years and <60 years at the time of diagnosis was not statistically significant (22% vs. 42%, respectively). The differences in the actuarial 5-year survival rate between the different treatment modalities were not statistically significant.

TABLE V. Treatment Modalities in Relation to FIGO* Staging of Patients With Uterine Sarcoma (n = 36)

Stage	Surgery[a] alone	Surgery[a] & RT[b]	Surgery[a] & Chem[c]	Surgery[a] & RT[b] & Chem[c]	Chem[c] alone	No treatment	Total
I	9	4	5	4	-	-	22
II	-	-	1	-	-	-	1
III	1		1	2			5
IV	1		4	1	1	1	8
Total	11	4	11	8	1	1	36

*International Federation of Gynecology and Obstetrics.
[a]At least total abdominal hysterectomy.
[b]Pelvic radiotherapy.
[c]Systemic chemotherapy.

TABLE VI. Treatment Modalities in Relation to Histologic Type/Subtype of Patients With Uterine Sarcoma (n = 36)

Histologic type/subtype[a]	Surgery[b] alone	Surgery[b] & RT[c]	Surgery[b] & Chem[d]	Surgery[b] & RT[c] & Chem[d]	Chem[d] alone	No treatment	Total
LMS	3	-	7	3	-	-	13
MMS							
CS	1	3	-	3	-	-	7
MMMMT	2	1	2	-	1	1	7
ESS							
low grade	4	-	-	-	-	-	4
high grade	1	-	2	2	-	-	5
Total	11	4	11	8	1	1	36

[a]Chem, systemic chemotherapy; LMS, leiomyosarcoma; MMS, mixed mesodermal sarcoma; CS, carcinosarcoma; MMMMT, malignant mullerian mixed mesodermal tumor; ESS, endometrial stromal sarcoma.
[b]At least total abdominal hysterectomy.
[c]Pelvic radiotherapy.
[d]Systemic chemotherapy.

DISCUSSION

Sarcoma of the uterus is the fourth most common female genital tract malignancy in Israel after ovarian carcinoma, endometrial carcinoma, and carcinoma of the cervix [12,19]. Since the presently reported 36 uterine sarcomas accounted for 11.2% of all uterine corpus malignancies seen during the study period and since the incidence of uterine corpus malignancies in Israel has been reported to be ~10/100,000 women [19], it can be assumed that the incidence of uterine sarcomas in the south of Israel is ~1/100,000 women. In the present study, uterine sarcomas accounted for 11.2% of all uterine corpus malignancies, with the ESSs making up 25% of the cases. This does not exactly corroborate previous studies that demonstrated that uterine sarcomas account for only 3–7% of all uterine corpus malignancies, with the ESSs making up ~15% of cases [1,6]. Schwartz et al. [12] in their study of 104 new cases of uterine sarcoma diagnosed in Israel during the 7-year period of 1969–1975 have reported that the incidence of uterine sarcoma in Israel is 1.55/100,000 women >20 years of age and have speculated that since the incidence of uterine sarcoma in Israel is higher than that reported in the literature (0.67/100,000 women >20 years of age) [20], the disease is presumably more prevalent among Jewish than non-Jewish women. Although Arab-Beduins make up nearly 20% of the population in the south of Israel, we have observed that only two (5.6%) of the 36 patients were Arab-Beduin women. Although Jews of Asian-African origin (Sephardic) make up ~60% of the Jewish population in the south of Israel, we have noticed more women of European-American origin (Ashkenazi) (61.8%) than those of Asian-African origin (Sephardic) (38.2%) affected by the disease. The same trend has been shown by Schwartz et al. [12] for uterine sarcomas in Israel and by Schenker and Tal [21] for endometrial carcinoma in Israel. An increased incidence of uterine sarcomas following radiotherapy to the pelvis for either carcinoma of the cervix or a benign condition has been noticed, and the relative risk of developing uterine sarcoma following pelvic radiotherapy has been estimated to be 5.4 [1,12]. The time interval between radiotherapy and the developing of the uterine sarcoma usually ranged from 10 to 20 years. Most of the sarcomas developing after pelvic irradiation were MMS. Of a total of 504 patients with uterine sarcoma collated by Lurain and Piver [1] from eight series in literature, 42 (8.3%) had a history of prior pelvic radiotherapy. In the present series, none of the

TABLE VII. Distribution of Patients With Uterine Sarcoma According to Site of Recurrence (n = 18)*

Site of recurrence	No. of patients
Locoregional	
Central pelvis	6
Vagina	4
Urinary bladder	2
Pelvic side wall	1
Rectum	1
Distant	
Lung	8
Peritoneal cavity	8
Liver	6
Bowel	3
Para-aortic lymph nodes	3
Retroperitoneum	2
Inguinal lymph nodes	2
Bone (ribs and vertebra)	2
Spleen	1

*Some patients had more than one site of recurrence; therefore, the total number of patients adds up to more than 18.

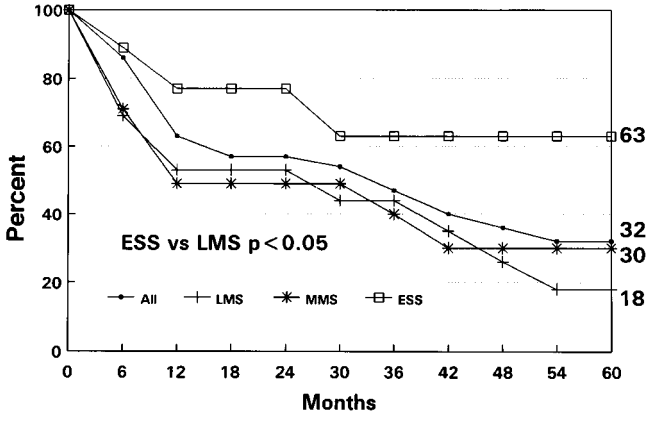

Fig. 1. Actuarial survival in relation to histologic type of patients with uterine sarcoma.

patients with uterine sarcoma had a history of prior pelvic radiotherapy.

Like others [10,12,13], we have demonstrated that on the average LMS tends to affect women in their early fifties, whereas ESS and MMS tend to affect women in their sixties. Thus patients with LMS tend to be ~10 years younger than patients with ESS and MMS. We could not demonstrate that age at the time of diagnosis was a factor affecting survival. The finding in the present series that 35 of the 36 patients were parous women with a mean parity of four children, corroborates previous studies that could not demonstrate that uterine sarcoma has a relationship with parity, as in endometrial adenocarcinoma [1].

Patients usually present with abnormal vaginal bleeding and uterine enlargement [1,22]. Diagnostic curettage (endometrial sampling) is reliable in making the diagnosis of sarcomas that arise from the endometrium (ESS and MMS), but is not reliable in making the diagnosis of a tumor that originates in the myometrium (LMS) [2]. In the present series, pre-operative diagnostic curettage missed the diagnosis in 24% of the patients in whom it was performed. This is in accord with findings in other series [4,12], confirming that pre-operative diagnostic curettage may miss the diagnosis of uterine sarcoma (especially LMS) in 20–75% of the patients. In the present series, in patients in whom diagnostic curettage had not been performed prior to explorative laparotomy and in patients in whom diagnostic curettage had missed the diagnosis of uterine sarcoma, the indication for laparotomy was either abnormal uterine bleeding or presumed leiomyoma or both. However, one should remember that the incidence of uterine sarcoma among patients operated on for presumed uterine leiomyoma and even among patients having surgery for ''rapidly growing'' leiomyoma is extremely low (0.23% and 0.27%, respectively) [23]. It is noteworthy that in none of the patients in the present series, surgery was performed because of a ''fast-growing uterus.''

Attention has been given to the various histologic types of uterine sarcoma in an attempt to identify those patients who are at greater or lesser risk for recurrence. It has been accepted that LMSs and MMSs each make up ~40% of uterine sarcomas followed by ESSs (15%) and other sarcomas (5%), although MMSs predominate in more recent reports [1]. Of a total of 1,440 patients with uterine sarcoma collated by Lurain and Piver [1] from 14 series in literature, 617 (42.8%) had LMS, 555 (38.5%) had MMS, 209 (14.5%) had ESS, and 59 (4.1%) had other sarcomas (Table III). We, like others [1,24], have demonstrated that: (1) LMSs and MMSs each made up more than a third of uterine sarcomas, (2) half of MMSs contained heterologous elements, with rhabdomyosarcoma the most frequent heterologous element identified, and (3) the most common carcinomatous element of MMS was endometrioid adenocarcinoma. With respect to histogenesis, recent evidence suggests that the sarcomatous component of MMS may be derived by conversion from the epithelial component [25,26]. Consequently, MMS may be more closely related to carcinoma than to sarcoma [25,26]. The prognostic significance of the histologic type of uterine sarcoma is still a matter of discussion. Some authors [27] could not demonstrate significant differences in 5-year survival between the various histologic types, whereas others [28] have found a better survival for ESS as compared with LMS and MMS. We have found a significantly better 5-year survival for ESS as compared with LMS and a trend for a better 5-year survival for ESS as compared with MMS.

Mitotic count, especially in patients with LMS and ESS, has generally been considered to be a significant

predictor of survival [29]. However, in this series, although a worsening in survival of patients with LMS and ESS was demonstrated with increasing mitotic count, it was not statistically significant.

We have observed that the majority of patients with uterine sarcoma are diagnosed in Stage I. Of a total of 876 patients with uterine sarcoma that we have collated from six series in recent literature [2,5,8,12,29,30], 527 (60.2%) had Stage I, 87 (9.9%) had Stage II, 147 (16.8%) had Stage III, and 115 (13.1%) had Stage IV (Table III). Many authors [5,12] have demonstrated that stage of disease at time of diagnosis is the most important factor affecting prognosis. However, although we have demonstrated a worsening in survival of patients with uterine sarcoma with advancing stage of disease, it was not statistically significant.

The relative rarity of uterine sarcomas has made assessment of the most effective management difficult [2,22]. In most studies reported to date, as in the present study, patients accrual occurred over a prolonged period of time during which treatment approaches and modalities changed. One rather unique aspect of the present study is, however, that all patients with uterine sarcoma from a well-defined geographical area could be included in the study and during the 34 years of the study period, no patient was lost to follow-up. The treatment of this disease has traditionally been modeled after that for endometrial adenocarcinoma with primary surgery consisting of total abdominal hysterctomy and bilateral salpingo-oophorectomy followed by postoperative adjuvant pelvic radiotherapy being the mainstay of treatment [2,30]. Removal of the ovaries during primary surgery for uterine sarcomas is justified since these tumors have a propensity for spreading to the ovaries (ovarian metastases have been noticed in ~10% of patients with early-stage uterine sarcoma) and a possible stimulating effect of estrogen from the retained ovaries on the tumor cells has been entertained [8,28,31–33]. Although lymph node metastases have been reported to range from 15% to 45% in patients with disease clinically confined to the uterus, the practical value of staging with lymphadenectomy is debatable since knowledge of lymph node status has minimal impact on the clinical management of women with uterine sarcoma [1,4]. Since most patients treated for uterine sarcomas die of distant metastases, the value of postoperative adjuvant pelvic radiotherapy has been questioned [2,34]. Some authors [2,3,10,35] have claimed that there is no definitive evidence that pelvic radiotherapy is beneficial even in preventing pelvic recurrence, whereas others [30] have suggested that postoperative adjuvant pelvic radiotherapy may be effective in preventing pelvic recurrence. ESS and MMS are reputed to be more radiosensitive than LMS [31,34]. Bokhman et al. [8] have shown that postoperative adjuvant pelvic radiotherapy exerted a positive prognostic effect on patients with ESS and MMS, whereas it was not justified in patients with LMS. Although the use of postoperative adjuvant chemotherapy has been an attractive concept [11], the validity of adjuvant chemotherapy in uterine sarcomas has remained uncertain and has yet to be demonstrated [1,8,10,30,31,36]. Some authors [31] have reported treatment of recurrent ESSs with progestins and noted response rates in the range of 50% [37]. In the present study, the addition of radiotherapy and/or chemotherapy to surgery did not significantly improve survival.

We have found that although more than half of the patients were diagnosed in Stage I, the ovarall 5-year survival rate was only 32%. This finding corroborates previous studies that demonstrated that the overall 5-year survival rate for patients with uterine sarcoma ranged from 26% to 38% [1,2,5,12,13,30,35]. We, like others [1,3], have found that the most common sites of recurrent disease were the central pelvis, intraperitoneal cavity, lung, and liver.

In conclusion, uterine sarcomas are uncommon and are generally considered to be aggressive tumors with propensity for local recurrence and distant metastases. Although most of the patients are diagnosed with tumor confined to the uterine corpus (Stage I), only about one-third of the patients survive 5 years. The survival of patients with ESS is better than that of patients with LMS and MMS. The mainstay of treatment is surgery consisting of total abdominal hysterectomy and bilateral salpingo-oophorectomy. By and large, adjuvant pelvic radiotherapy is given in early-stage disease and adjuvant systemic chemotherapy is prescribed in advanced-stage disease. However, there is no definitive evidence that adjuvant therapy with pelvic radiotherapy or systemic chemotherapy improves survival. The place of adjuvant therapy in uterine sarcoma requires further evaluation.

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